# Progress on Global Standards for Medical Research

CDISC®

*Setting the Global Standard for Medical Research*

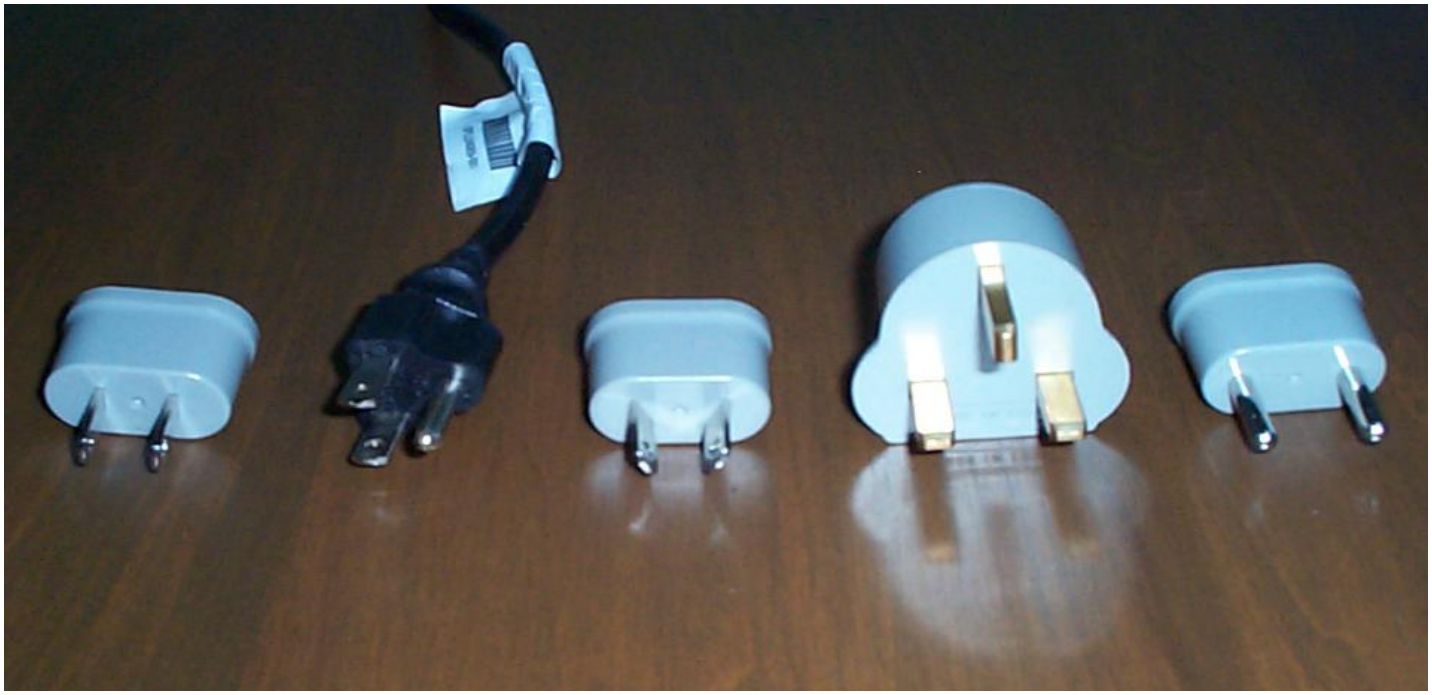
CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

**Biomedical Informatics Without Borders, Bethesda, MD**

**2-3 September 2008**

**Rebecca D. Kush, PhD**
**President & CEO, CDISC**

# Standards?



# Standards, Who Needs Them?

**USB 2.0 Specification**


**Red Book, IEC 908**

# Clinical Research Trends

- Clinical research becoming increasingly global
- Initiatives to improve safety monitoring
- Healthcare IT initiatives; use of EHRs and need for interoperability
- Government Regulatory Initiatives
  - US NIH CTSA referencing internal, intra-institution and external interoperability among research partners
  - FDA BIMO initiative to scale auditing and review 'quality system'
  - EU EMEA Inspectors interest in eSource audits at sites
- Need for transparency of clinical research information through publicly accessible registries and databases
- Investigative studies are still using multiple disparate tools

***Important role of data interchange standards in all of these***

***The mission of CDISC is to develop and support global,***

***platform-independent data standards that enable information system interoperability***

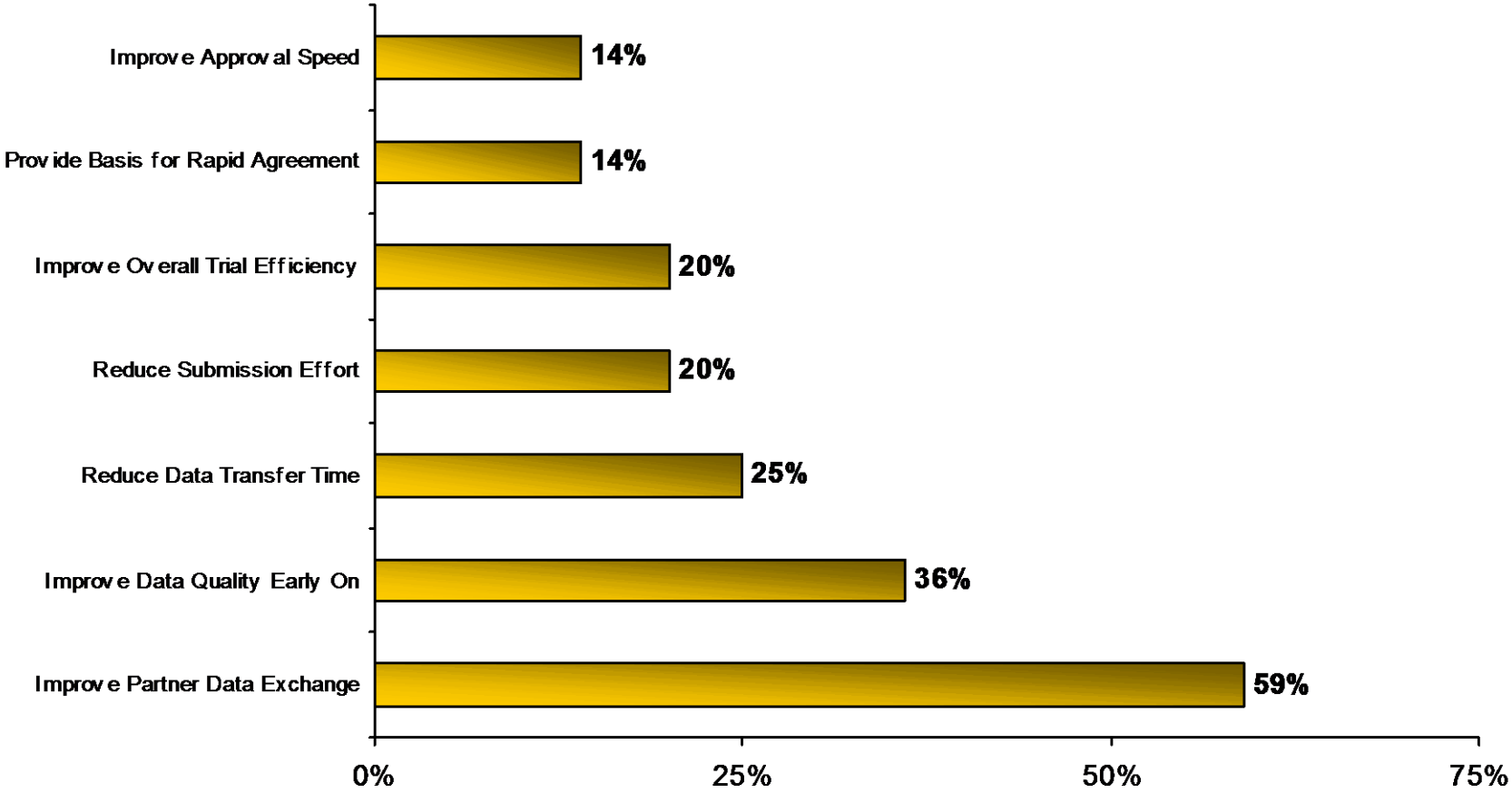
***to improve medical research and related areas of healthcare.***

# Clinical Data Interchange Standards Consortium (CDISC)

- Global, open, multidisciplinary, non-profit organization initiated in 1997 as a volunteer group
- Incorporated in 2000; now > 200 member organizations
  - Academic research centers
  - Global biopharmaceutical and device companies
  - Technology and service providers, etc.
- Active Coordinating Committees in Europe and Japan; one initiated in China
- ISO Liaison Status A
- Accepted into Joint Initiative Council JIC =
  - HL7/ISO/CEN collaboration

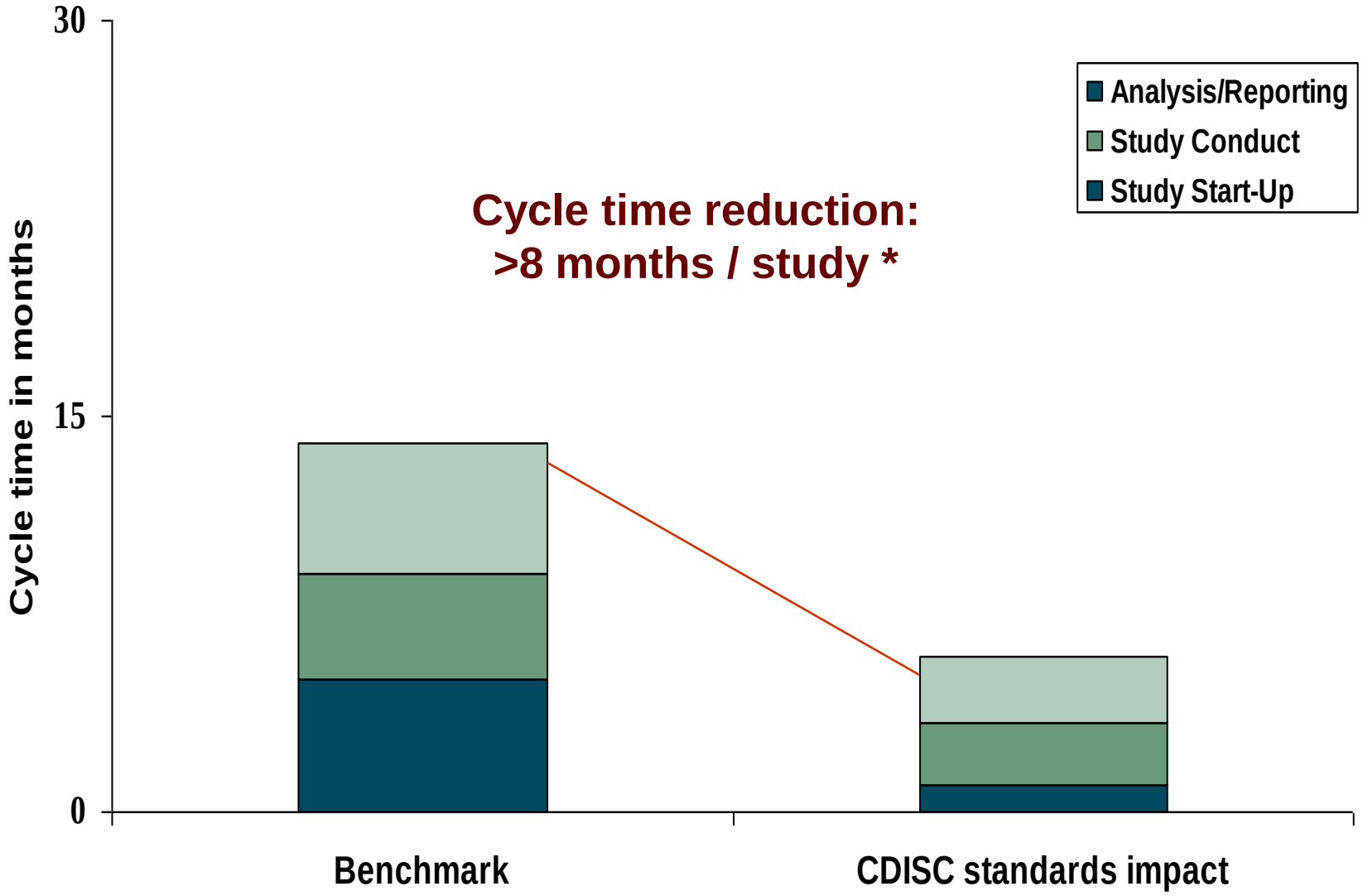
- Through a consensus-based approach (COP-001), CDISC has established worldwide industry standards to support the electronic acquisition, exchange, submission and archiving of clinical research data and metadata to improve data quality and streamline medical and biopharmaceutical product development and research processes.
- Standards are freely available on the CDISC website (www.cdisc.org); these are made possible by our generous members and dedicated participants.

# Top Perceived Benefits of Adopting CDISC Standards




*Source: Tufts CSDD-CDISC Study on ECT and Standards Adoption, 2007*

# Business Case – Cycle Time Savings




*Note: Aggregate/benchmark data, patient participation time not included

# CDISC Business Case (Gartner, PhRMA) – Summary Findings

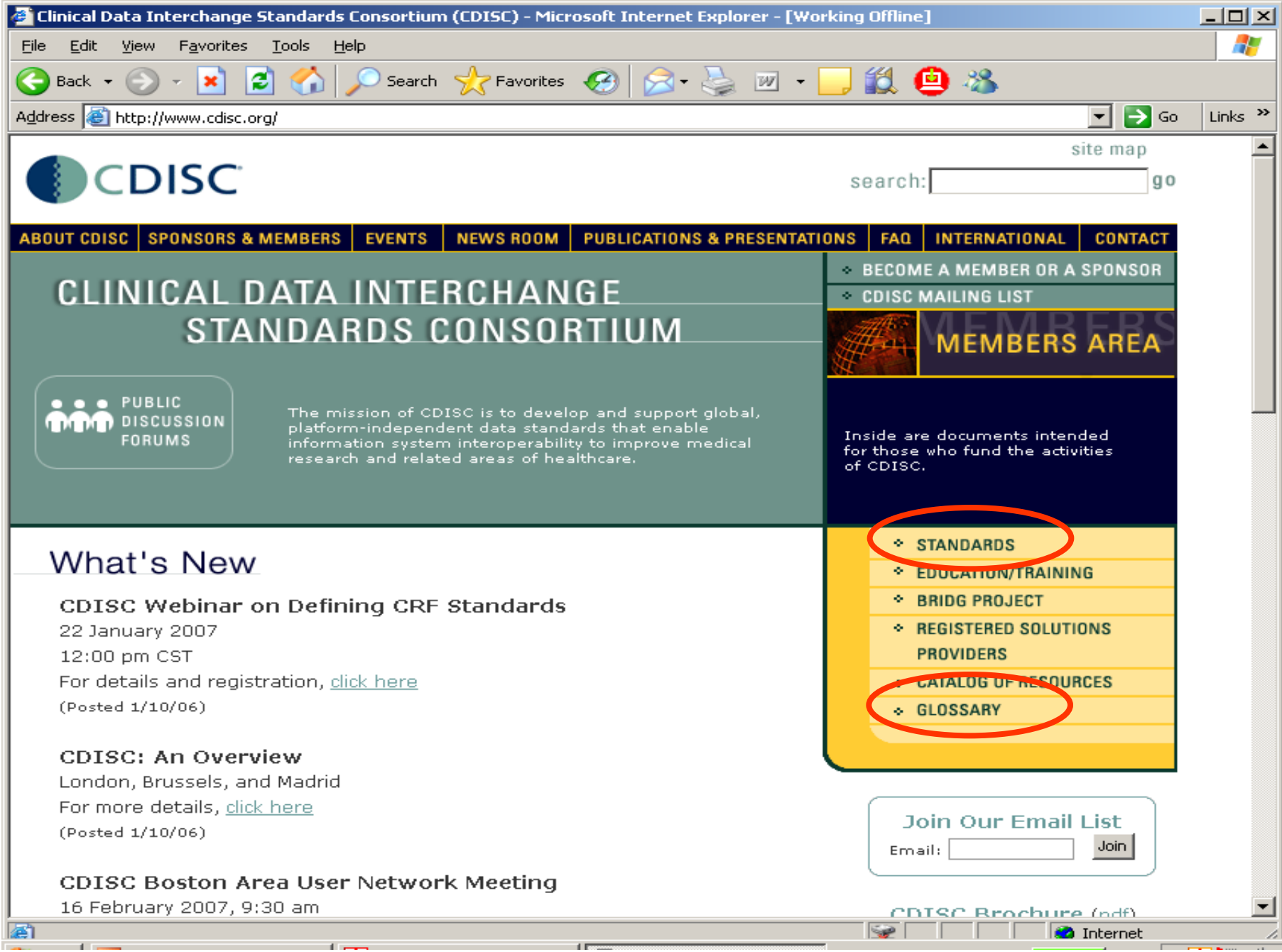
- CDISC standards can significantly improve processes, thus saving time and cost*
  - ***~ 60% of the non-subject participation time***
  - ***70-90%  (~ half the value) in the start-up stage***
- CDISC standards have additional benefits for clinical research
  - ***Increase data quality***
  - ***Enable data integration, enhancing re-usability in 'knowledge' warehouses to improve science, marketing and safety surveillance***
  - ***Streamline data interchange among partners***
  - ***Facilitate review of regulatory submissions***
  - ***Enable integration of data from disparate tools/technologies***
  - ***Improve communication among project team members***

**Note: Actual savings will vary per company and study, depending on baselines.*

# One Experience

*"We avoided the requirement to run 3 studies at a saving of around £15 million by conducting analyses of aggregated data; we got a paediatric indication for a drug approved by analysing aggregated data rather than by running a study/studies. In both cases, we saved considerable time to boot (undoubtedly >1 year, but maybe quite a bit more than that)."*

*Source: Simon Bishop, GSK.*


Clinical Data Interchange Standards Consortium (CDISC) - Microsoft Internet Explorer - [Working Offline]
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The mission of CDISC is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.
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Inside are documents intended for those who fund the activities of CDISC.
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CATALOG OF RESOURCES
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What's New
CDISC Webinar on Defining CRF Standards
22 January 2007
12:00 pm CST
For details and registration, click here
(Posted 1/10/06)
CDISC: An Overview
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For more details, click here
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CDISC Boston Area User Network Meeting
16 February 2007, 9:30 am
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Internet


Source: S. Kenny,
ADaM Team Leader

| Standard | Description | Implementation Version Release Date |
|---|---|---|
| **SDTM, SEND** | Ready for regulatory submission of CRT<br>Over 12,000 downloads as of Apr 08 | 2004* |
| **ODM** | CDISC Transport Standard for acquisition, exchange, submission (define.xml) archive | 2001* |
| **Define.xml** | Case Report Tabulation Data Definition Specification | 2005* |
| **LAB** | Content standard – available for transfer of clinical lab data to sponsors | 2002 |
| **ADaM** | General Considerations document and examples of datasets for submission | 2004 |
| **Protocol Representation** | Collaborative effort to develop machine-readable standard protocol with data layer | In progress-due in 2008 |
| **Terminology Codelists** | Developing standard terminology to support all CDISC standards | 2006 (Pkg1 & 2A)<br>Pkg 2B in progress |
| **CDASH** | Data acquisition (CRF) standards | In progress-due in 2008 |

*** Specification referenced via FDA Final Guidance**

# Data Flow Using CDISC Standards

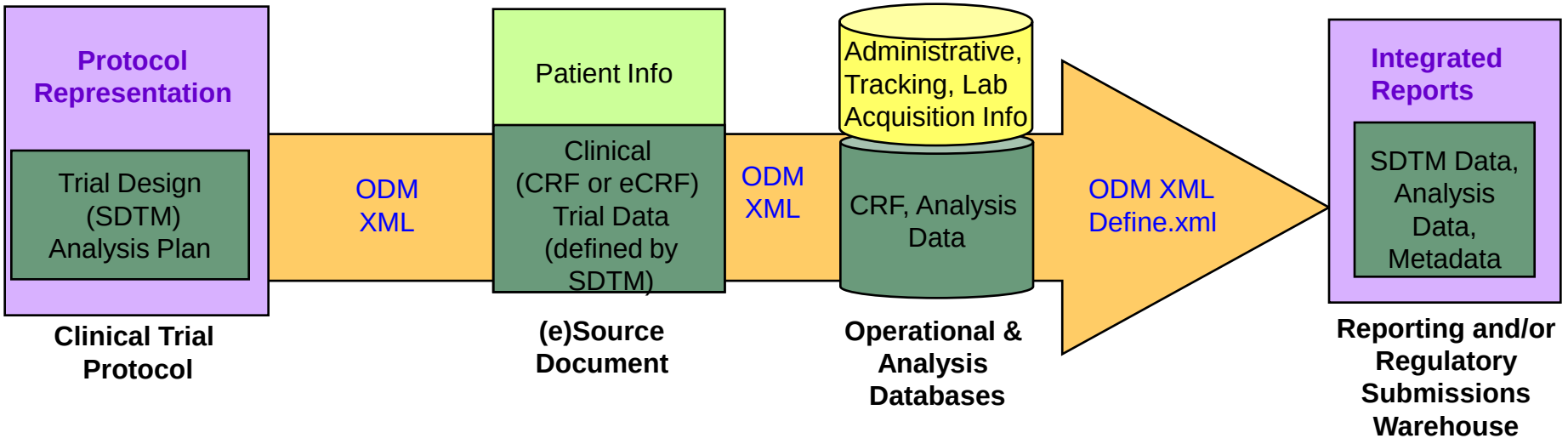
= ODM - Operational Data Model (transport)

= SDTM - Study Data Tabulation Model and ADaM - Analysis Dataset Model (content)
SEND for Non-clinical Data

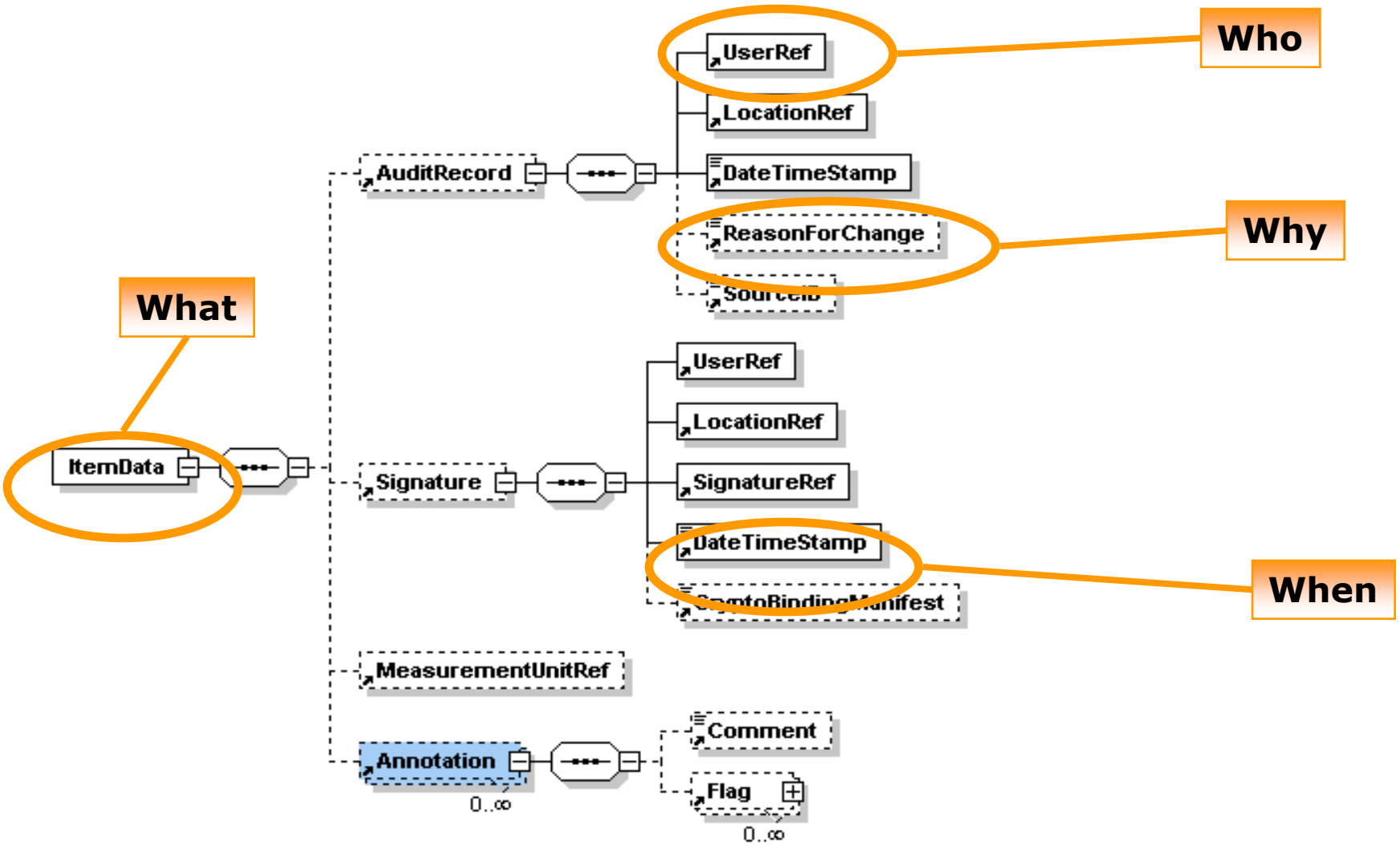
= Protocol Representation Standard (content)

= LAB – Laboratory Data Standard

= Source data
(other than SDTM/CRF data)

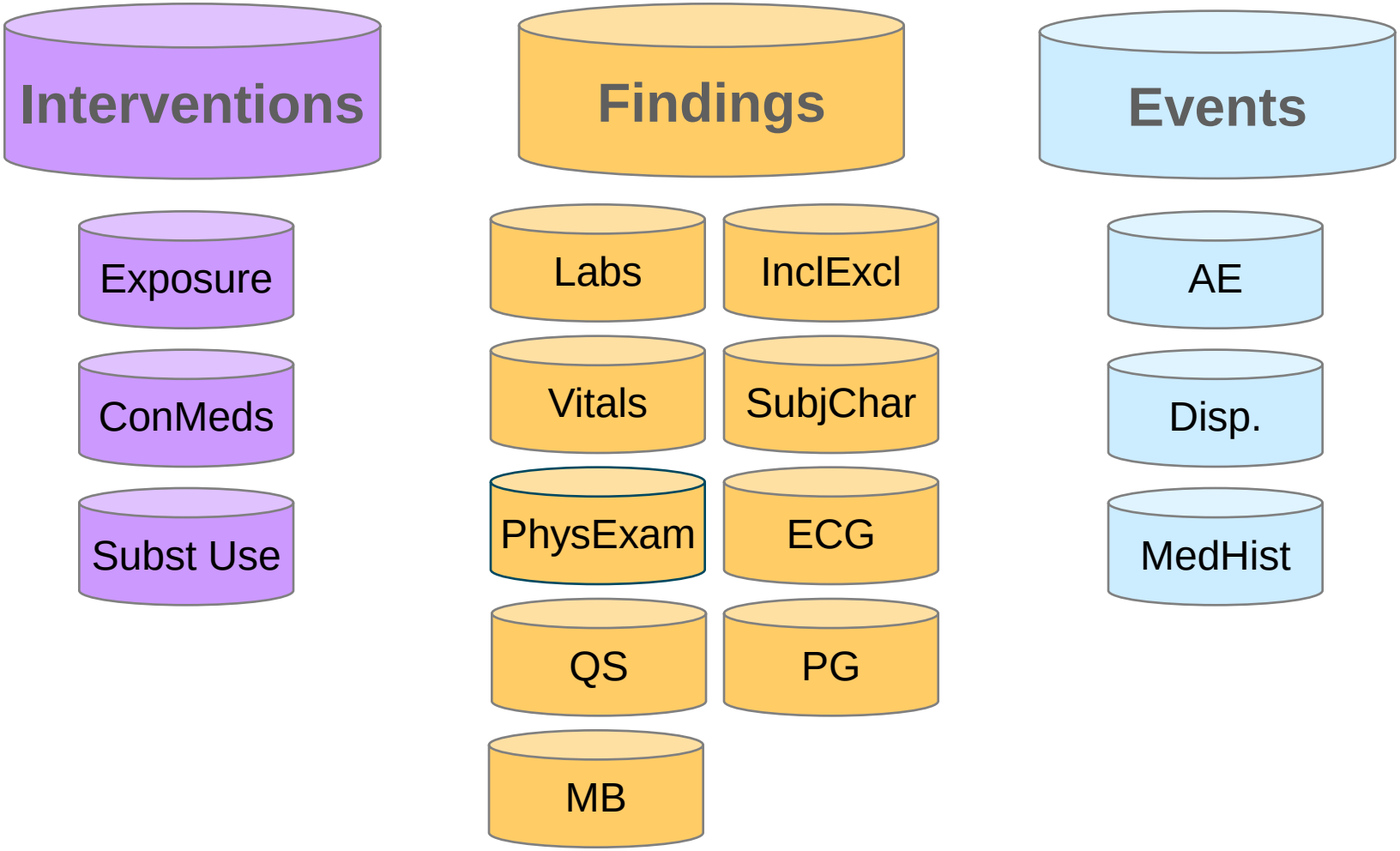


# CDISC ODM & Audit Trail




*Slide courtesy Dave Iberson-Hurst, Assero*

# Study Data Tabulation Model (SDTM)



# FDA endorses CDISC standards by including them as specifications in FDA Final Guidance

U.S. Food and Drug Administration

Department of Health and Human Services

FDA Home Page | Search FDA Site | FDA A-Z Index | Contact FDA

**FDA News**

FOR IMMEDIATE RELEASE
P04-73
July 21, 2004

Media Inquiries: 301-827-6242
Consumer Inquiries: 888-INFO-FDA

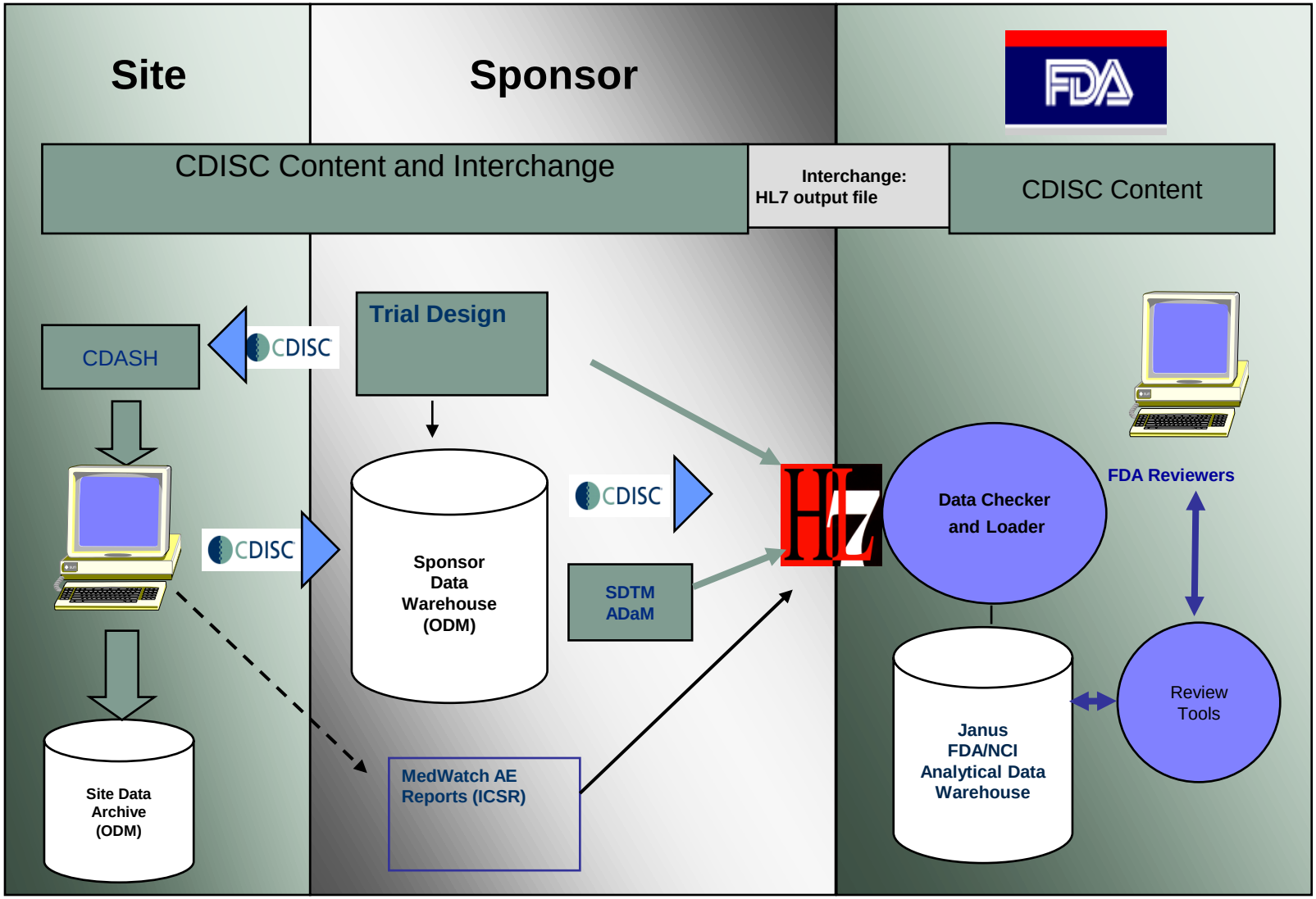
**FDA Announces Standard Format That Drug Sponsors Can Use to Submit Human Drug Clinical Trial Data**

The Food and Drug Administration (FDA) today announced a standard format, called the Study Data Tabulation Model (SDTM) developed by the Clinical Data Interchange Standards Consortium (CDISC), that sponsors of human drug clinical trials can use to submit data to the agency. It is expected that this step will lead to greater efficiencies in clinical research and FDA reviews of New Drug Applications (NDAs).

**Study Data Tabulation Model, define.xml (CRTDDS), Operational Data Model (ODM): Specifications for FDA implementation of the ICH eCommon Technical Document – Final Guidance**

**October 2005 – Federal Register Notice of Proposed Rule and listed as DHHS Priority**

# From FDA 5-yr IT Plan



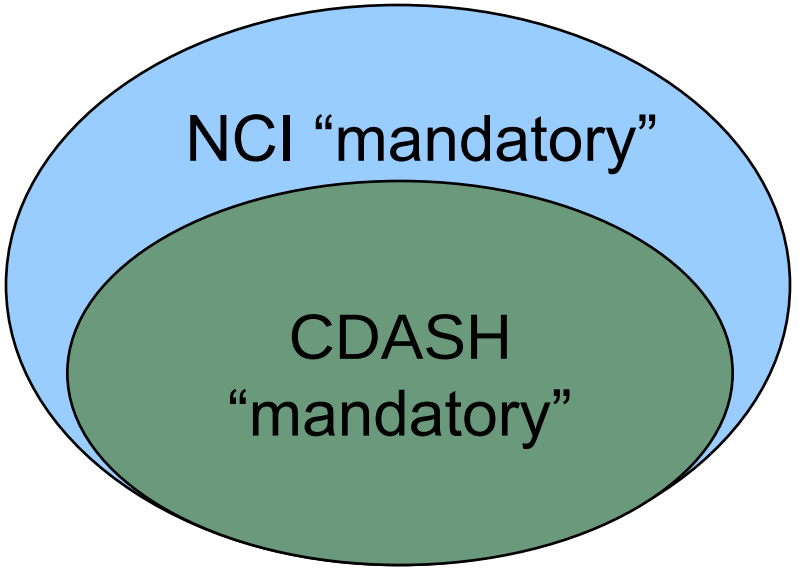
Strength *through collaboration…*

# Clinical Data Acquisition Standards Harmonization

- Addresses FDA Critical Path Opportunity #45 – Streamline Data Collection at Investigative Sites
- Continuation of work initiated with FDA by Association of Clinical Research Organizations (ACRO)
- Supported by a Collaborative Group of **17** Organizations
  - Core Team of **16**
    - **11** Working Groups
    - Comprised of between **8-40** volunteers
  - ~**190** Working Group Volunteers
  - **16** Safety Data Domains Developed
    - organized into **4 "Packages"**
- V1.0 Release September 2008

# CDASH and caBIG CRF Harmonization: Complementary Activities

- The CDISC CDASH initiative and the NCI/caBIG Case Report Form (CRF) Harmonization and Standardization Project are both concerned with harmonizing and standardizing the collection of data in clinical trials, but their focus and granularity differ somewhat
  - CDASH's efforts are focused on elements that are common to all clinical trials
  - caBIG is focused on trials in the oncology space
- NCI/caBIG CRF modules will (at a minimum) include all CDASH "mandatory" questions plus additional content that is essential in the oncology space.



# NCI caBIG – CDISC CDASH Collaboration Mechanisms

- Mutual Staffing Support
  - NCI/caBIG is providing staff to many CDASH “streams”
  - CDASH project director (Rhonda Facile) sits on the NCI Task Force that manages the CRF project
- Project Inputs
  - Where CDASH streams complete before NCI CRF modules are defined, the CDASH module is one of the inputs to the NCI working groups and vice versa
- Terminology and Metadata Support
  - NCI Enterprise Vocabulary Services (EVS) provides terminology support for CDISC/CDASH
  - NCI cancer Data Standards Repository (caDSR) provides a repository to maintain CDISC/CDASH data elements

# “Standard” Controlled Terminology

Global Pharma & CROs

FDA & Academia


International SDOs

Vocabulary Developers

*Health Level Seven*
*(RCRIM TC)*

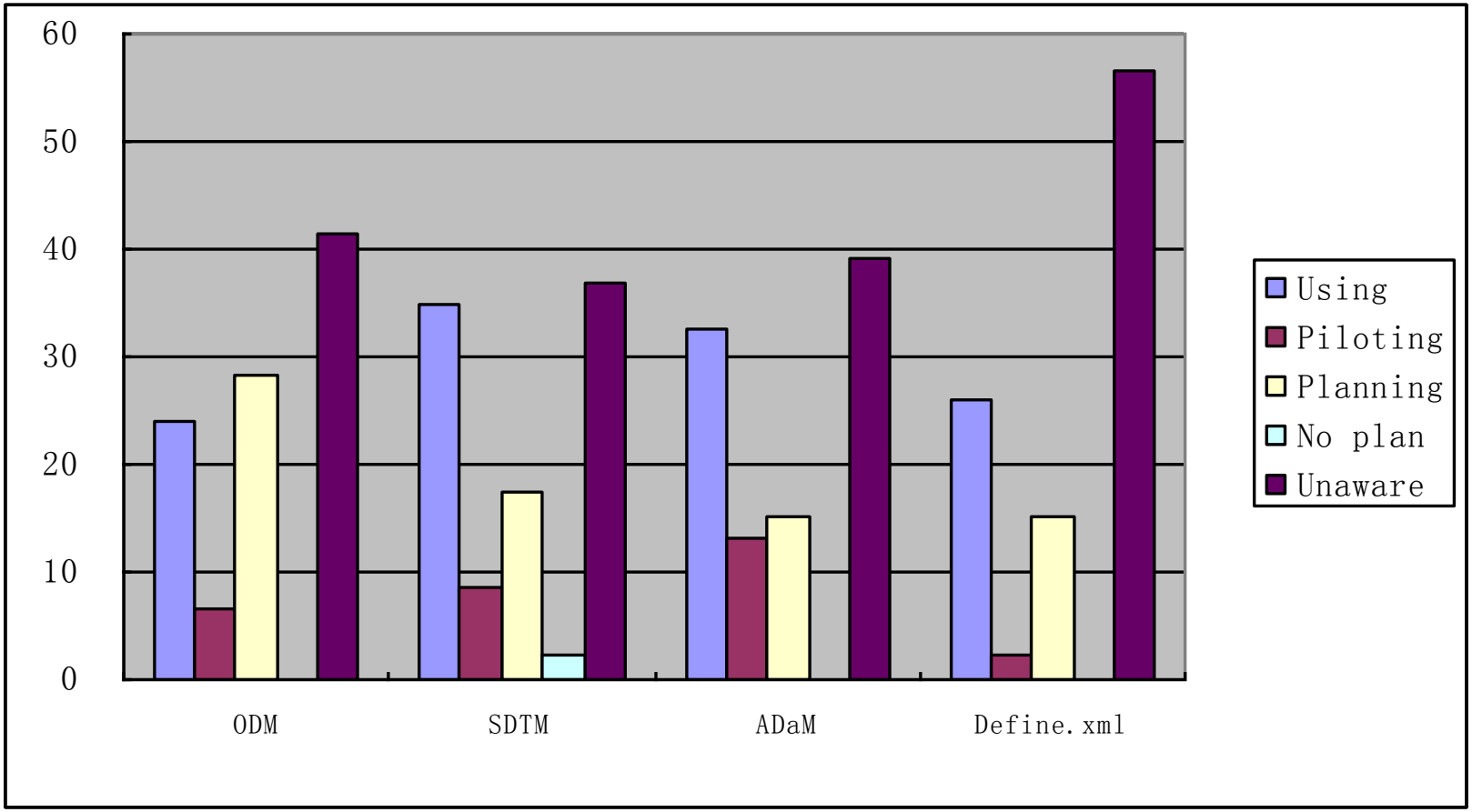
# *European Medicines Agency (EMEA)*

- The EMEA's GCP Inspectors Working Group released their "*Draft Reflection Paper on Expectations for Electronic Source Documents"* which references the CDISC eSource Data Interchange initiative:
  - http://www.emea.europa.eu/Inspections/docs/50562007en.pdf
- ICH (especially EMEA) have invited CDISC (and NCI) to collaborate on the ICH-ISO Terminology Initiatives; CDISC leading 2 teams
- EudraCT and CDISC
  - EMEA has provided their EudraCT specifications to CDISC for harmonization with the Protocol Representation elements
  - EMEA invited CDISC to have a European CDISC representative on their EudraCT Joint Operational Group (JOG), which falls within their Telematics Implementation Groups (TIGs).
- Looking at how to work together to align the EMEA's Reference Data Model (RDM) with Biomedical Research Information Domain Group (BRIDG) model.

# *Japan Ministry of Health, Labor and Welfare (MHLW)*

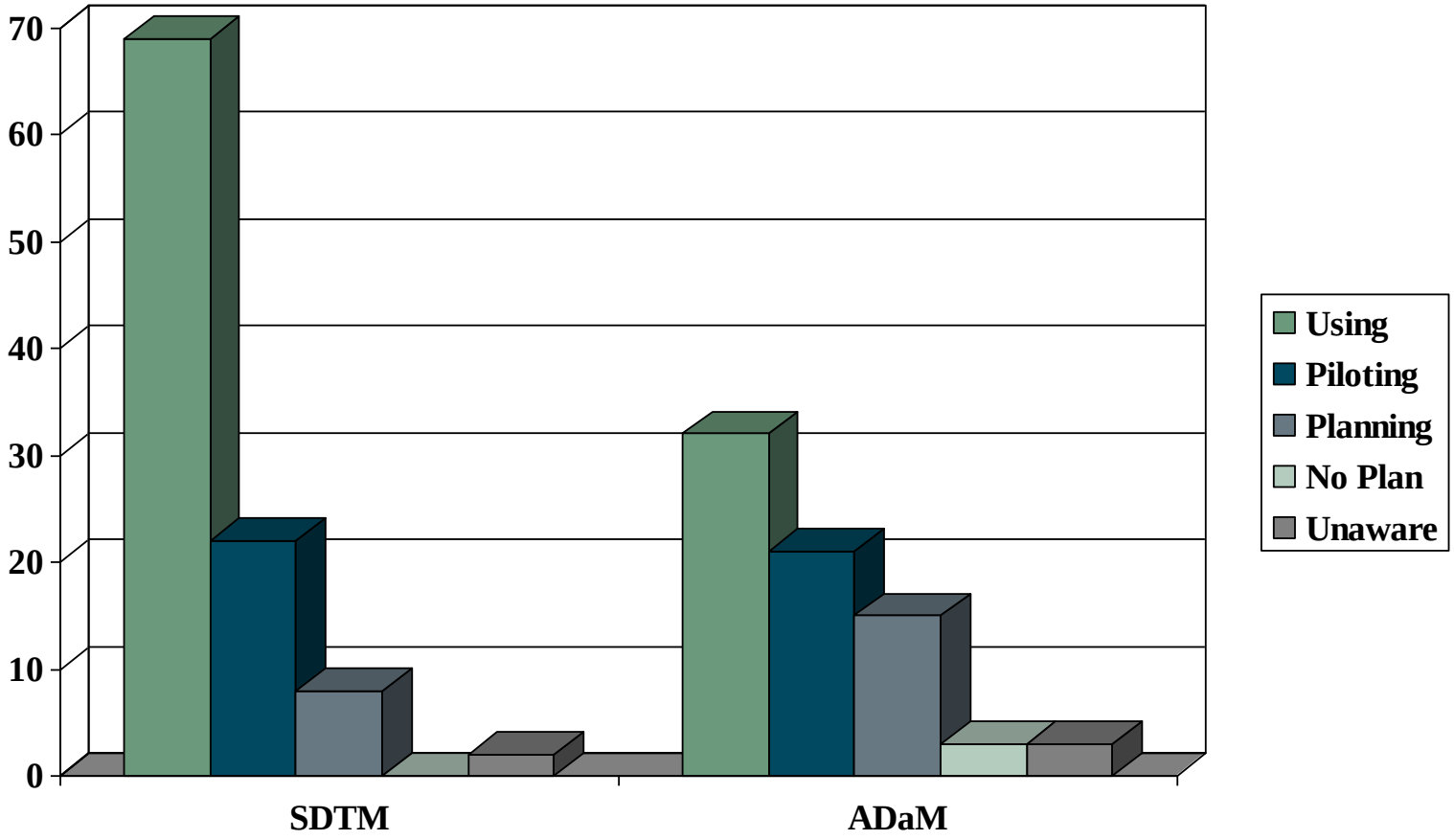
- CDISC is now referenced in the MHLW 5-year eClinical Trial Initiative
  - Forty sites selected to promote the initiative
  - MHLW requested J3C assistance in development of proposal for the plan for implementation to begin in ~ April 2008
- MHLW Keynote speakers at Japan Interchange (May 2007 and June 2008)

# Adoption of CDISC ODM, SDTM, ADaM and Define.xml in China



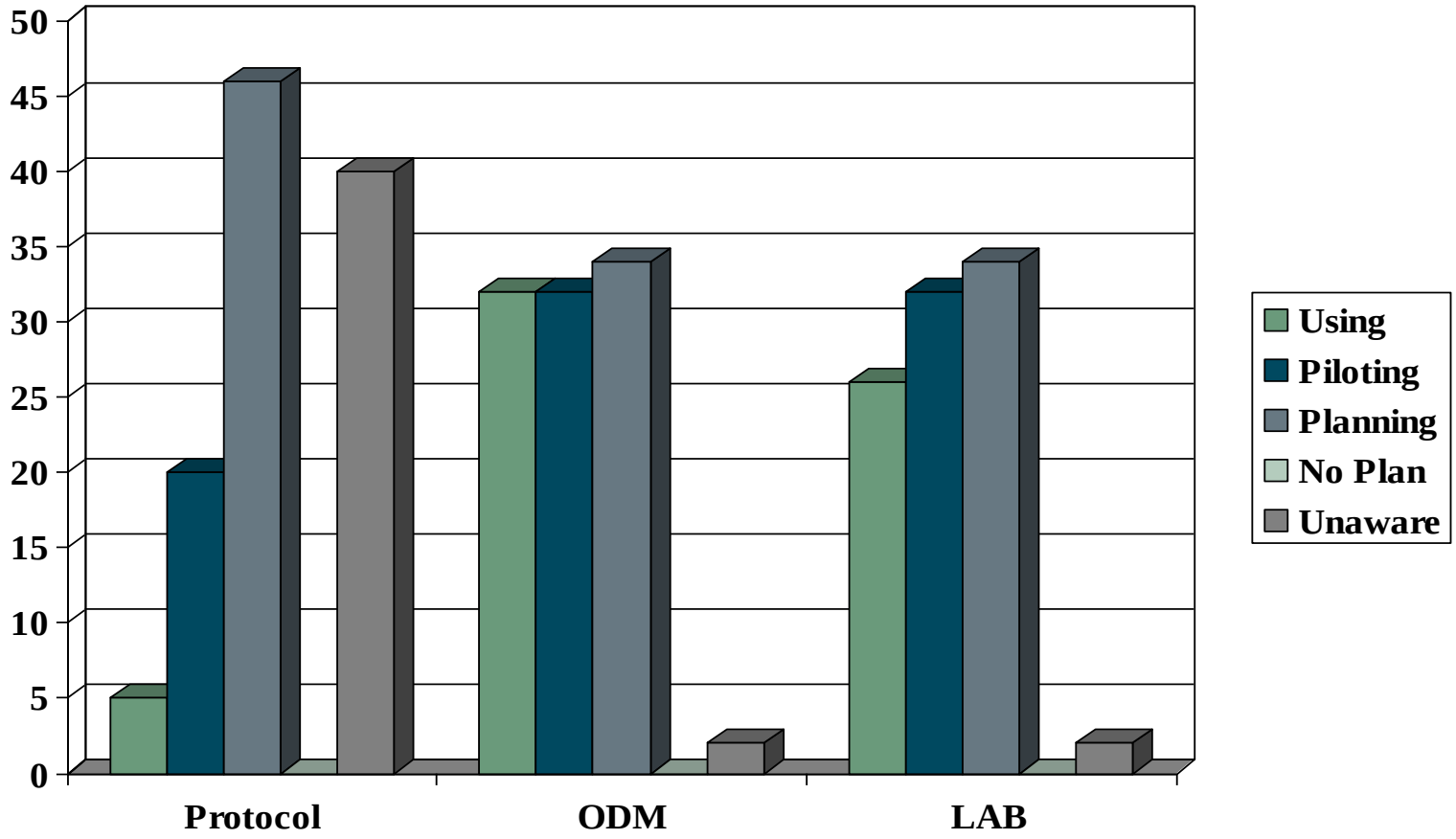

ISBS 2008 (Zibao Zhang)

# Adoption of CDISC SDTM, ADaM



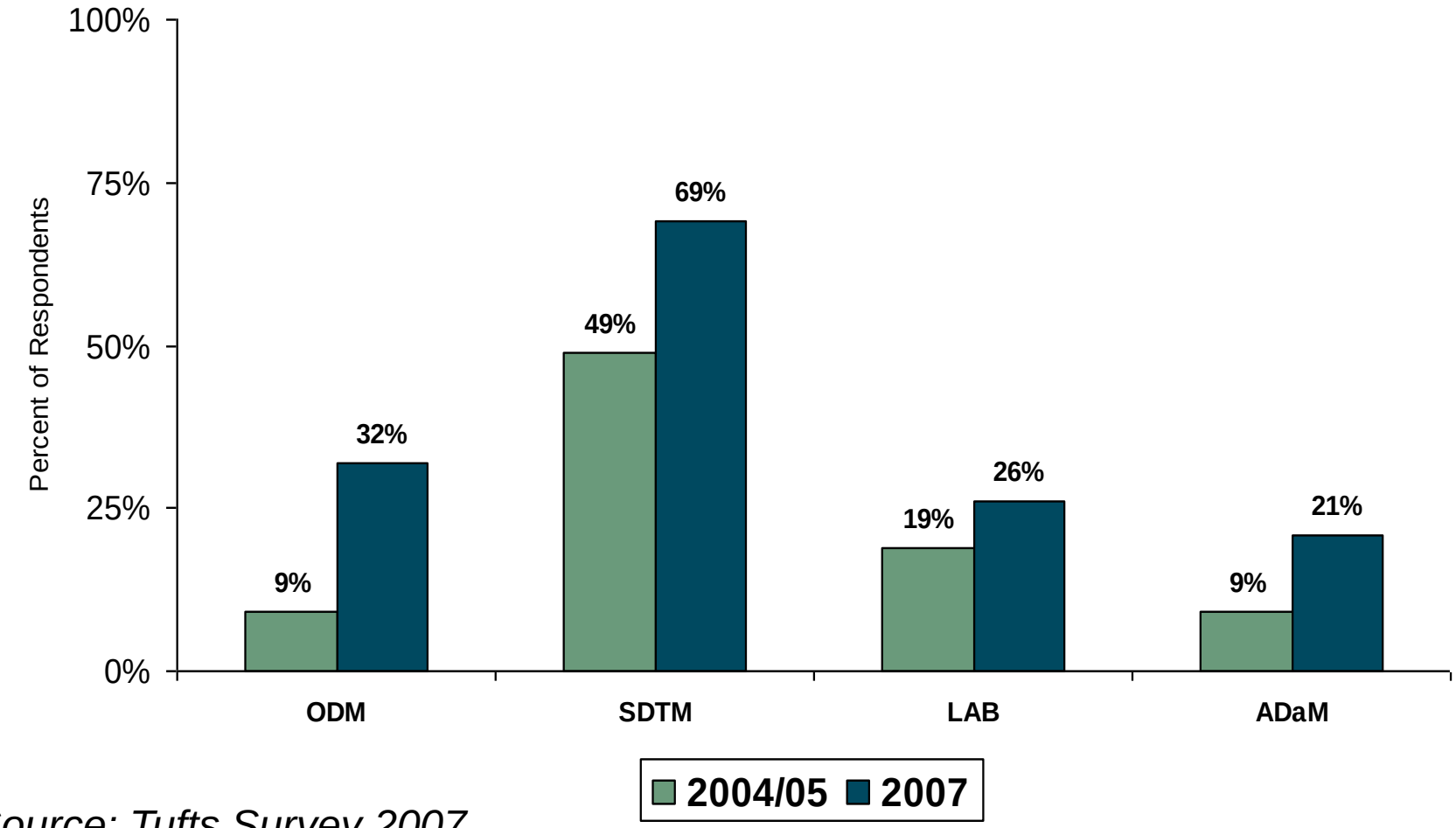

Tufts Research - 2007

# Adoption of CDISC Protocol Representation, ODM, LAB




Tufts Research - 2007

# Increasing Usage of CDISC Standards




*Source: Tufts Survey 2007*

# Initiatives Towards the CDISC Mission of Interoperability and Linking Research with Healthcare

- CDISC-HL7 Charter Agreement since 2001, with commitment to harmonized standards for clinical research and healthcare
- BRIDG Model
- eSource Data Interchange Initiative
- Healthcare Link and Integrating the Healthcare Enterprise (IHE) Integration Profile

# The BRIDG Model*

*A clinical research domain analysis model (UML)*
*initiated by CDISC,* ***BRIDGing***

- ***Organizations (CDISC, HL7, FDA, NCI)***
- ***Standards***
- ***Research and Healthcare***

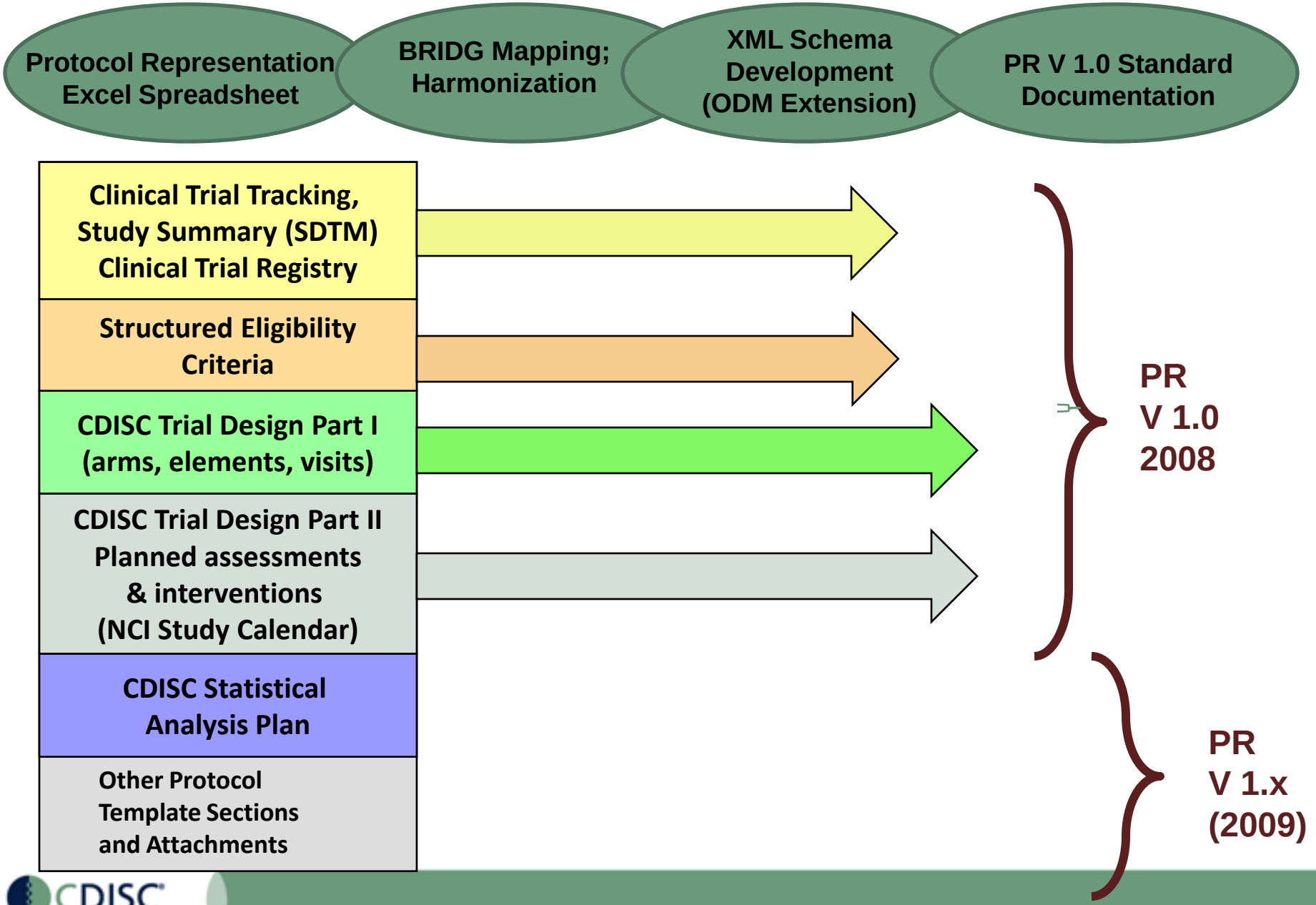
*Towards semantic interoperability; a Portal to Healthcare*

*Open source ; Collaborative Project*

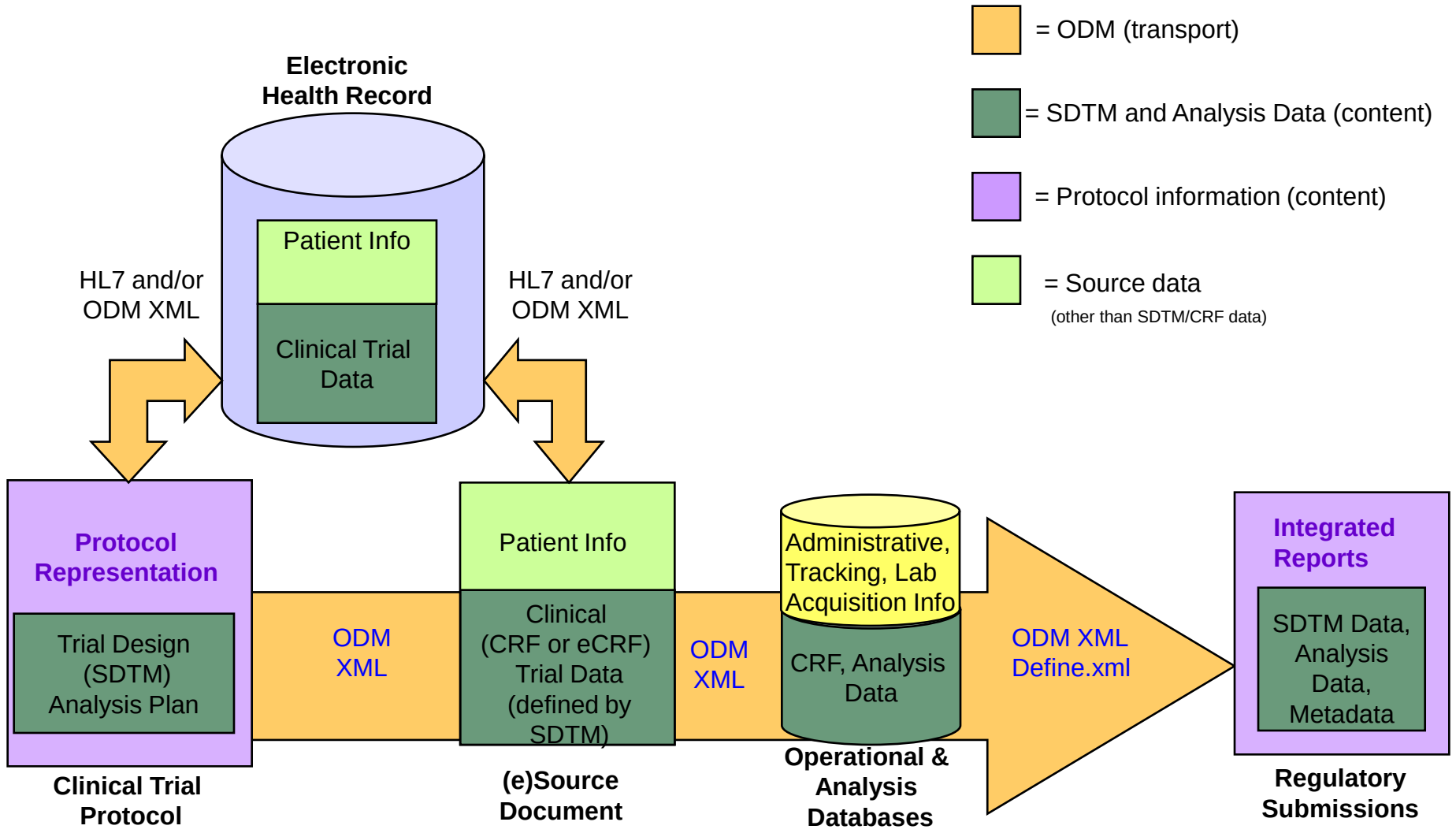
- *See BRIDG Model on CDISC website*
  *or www.bridgmodel.org*

***Biomedical Research Integrated Domain Group (BRIDG) Model**

# Protocol Representation Standard - Development



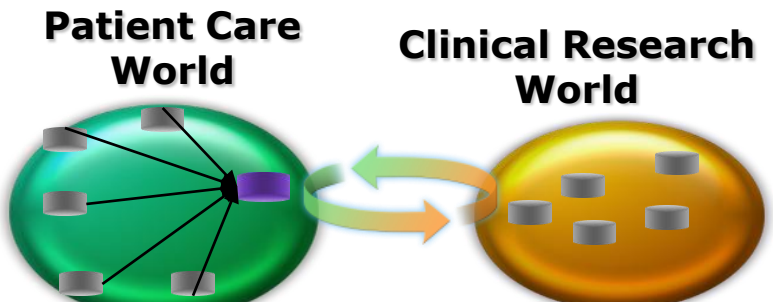
# Data Flow Using CDISC Standard Linking Clinical Research and Healthcare



# eSource Data Interchange (eSDI) Initiative

- **Purpose of eSDI Initiative**
  - *to facilitate the use of electronic technology in the context of existing regulations for the collection of eSource data in clinical trials for regulatory submission by leveraging the power of the CDISC standards, in particular the Operational Data Model (ODM).*
- **Overarching goals:**
  - to make it easier for physicians to conduct clinical research,
  - collecting data only once in an industry standard format for multiple downstream uses, and thereby
  - to improve data quality and patient safety
- **Product** (2 year development process)
  - *Version 1.0 document posted at www.cdisc.org (Presentations and Publications); Includes Requirements, Scenarios, Checklists…*
- **EMEA Document (GCP Inspectors):** REFLECTION PAPER ON EXPECTATIONS FOR ELECTRONIC SOURCE DOCUMENTS USED IN CLINICAL TRIALS

# CDISC Initiative: Healthcare Link





2004: Proof of Concept: Demonstrated interoperability between Electronic Health Records and Clinical Research Systems using open standards.

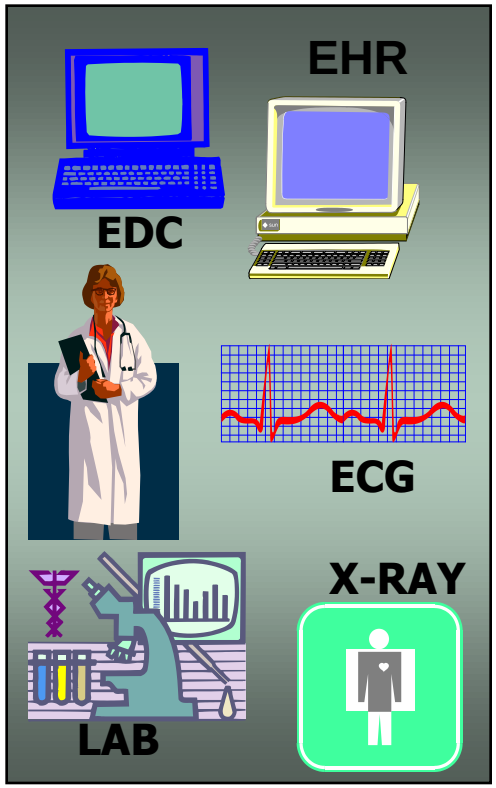
2006- present: Development, Demonstration and Implementation of an Integration Profile called Retrieve Form for Data Capture (RFD) → using EHRs to do Clinical Research and Safety Reporting; 5 use cases demonstrated at HIMSS.

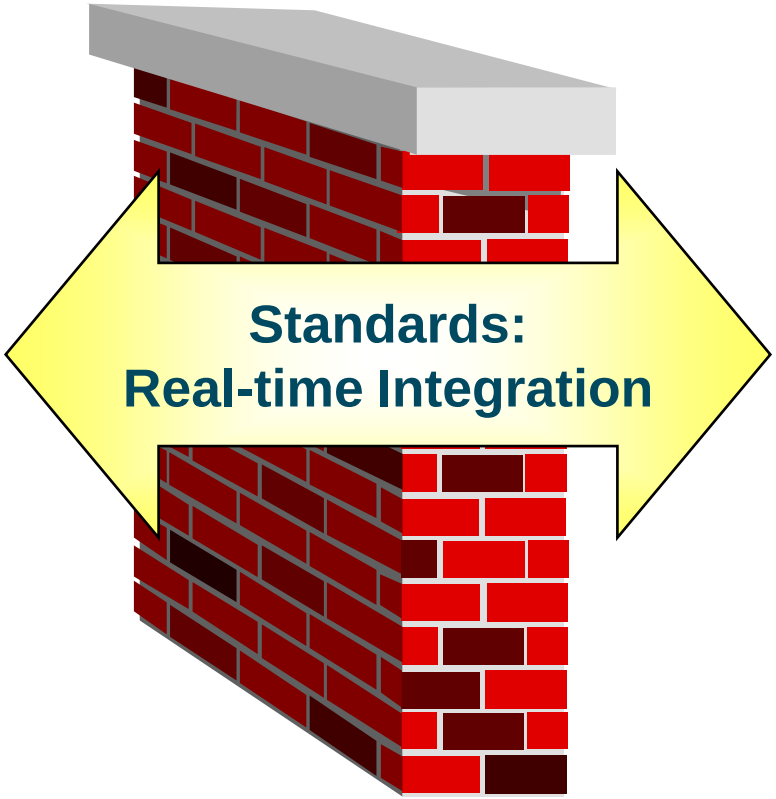
2008: RFD used with coming CDASH Standard to define CRFs for data acquisition from Electronic Health Records

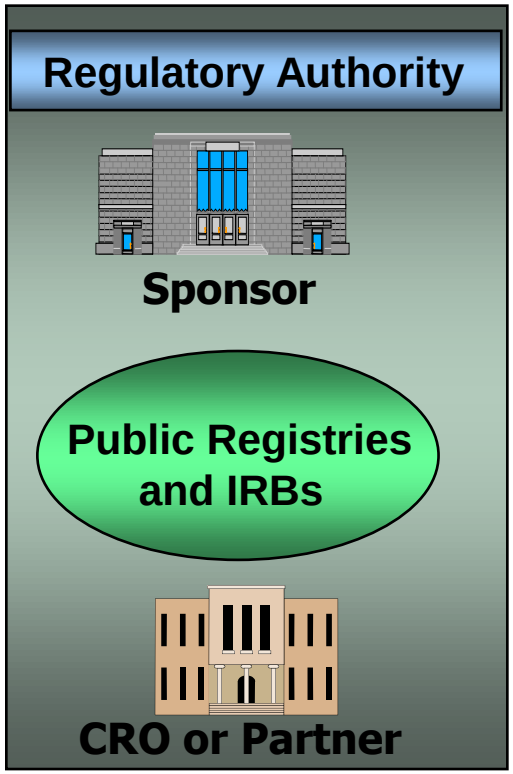
# Vision – Medical Innovation

Collect Data Once,
(Various Sources)

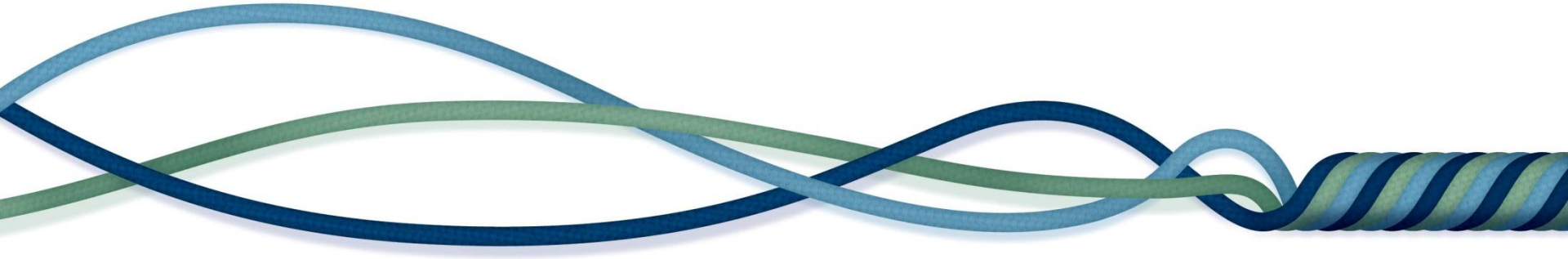
"Rolling Warehouse"
Multiple Downstream Uses



*CDISC operates to advance the continued improvement of public health by enabling efficiencies in medical research and related areas of healthcare.*



# Strength *through collaboration.*

*As a catalyst for productive collaboration, CDISC brings together individuals spanning the healthcare continuum to develop global, open, consensus-based medical research data standards.*